CHAPTER 49
Coronary Artery Disease

KEY TEACHING POINTS

- In the evaluation of patients with chronic intermittent chest pain and suspected coronary artery disease, the most helpful bedside finding is the patient's description of pain (i.e., typical angina, atypical angina, or nonanginal chest pain). In these patients the following findings increase probability of coronary disease, but only modestly: an ankle-to-arm pressure index of 0.9 or less, arcus senilis, and the earlobe crease.
- In the evaluation of patients with sustained chest pain and suspected myocardial infarction, the most helpful bedside finding is the electrocardiogram. In these patients the following findings increase probability of myocardial infarction: systolic blood pressure less than 100 mm Hg, the third heart sound, jugular venous distention, diaphoresis, and crackles.
- The finding of chest wall tenderness *decreases* probability of myocardial infarction in patients with sustained chest discomfort being evaluated in the emergency department, but it is unhelpful when evaluating chronic intermittent chest pain in the clinic.
- In patients with suspected myocardial infarction, the response to nitroglycerin and to GI cocktail is unhelpful.
- In patients with suspected acute coronary syndromes, the following combination of findings identifies a group of patients at very low risk for complications in the next 24 hours: an electrocardiogram without ST/T wave changes, pain severity that is less severe than prior angina, the absence of hypotension, and the absence of crackles.

I. INTRODUCTION

Coronary disease is the leading cause of heart disease and death in the United States,[1] and chest pain accounts for 8% to 10% of complaints of patients presenting to clinics or emergency departments.[2-4] The bedside diagnosis of chest pain is difficult and at times humbling, as illustrated by up to 1% to 8% of patients with myocardial infarction (confirmed by cardiac biomarkers) being misdiagnosed and discharged home from emergency departments.[5-12] The focus of this chapter is to identify all aspects of the initial patient encounter—patient interview, physical examination, and the electrocardiogram—that help to distinguish patients with angina and myocardial infarction from those with mimicking disorders.

The first clear description of **angina pectoris** was given in 1768 by William Heberden, who coined the term* and provided a clinical description that has been unsurpassed. Just 8 years later, Edward Jenner linked angina to "ossification" of the coronary arteries and insufficient coronary blood flow,[13] and in 1878 (more than 50 years before the introduction of electrocardiography), Adam Hammer correctly diagnosed the first case of myocardial infarction during life in a young man with sudden collapse, bradycardia, and enfeebled heart tones.[14,15] Coronary disease was once considered to be an uncommon disorder—the great 19th century American cardiologist Austin Flint found only seven cases of angina in his clinical records[16] and Osler personally observed only 40 cases during his career.[13]

II. THE FINDINGS

A. INTRODUCTION

Unlike other clinical problems in cardiology, such as valvular disease and heart failure, patients with coronary artery disease have few or no physical findings. For more than 100 years, the most important aspect of diagnosing coronary disease has been the patient's description of chest pain, whereas the most important element in diagnosing myocardial infarction (at least since 1918) has been the electrocardiogram.

B. DESCRIPTION OF CHEST PAIN

Heberden wrote that **angina** is a "most disagreeable sensation in the breast" that seizes patients "while they are walking" yet vanishes "the moment they stand still."[17] Modern definitions of **typical angina** retain most of Heberden's essential features, by defining it as substernal discomfort with three characteristics: it (1) is precipitated by exertion, (2) is improved by rest or nitroglycerin (or both), and (3) lasts less than 10 minutes. Many patients also describe radiation of the pain to the shoulders, jaw, or inner aspect of the arm. In contrast, **atypical angina** is substernal discomfort with atypical features (e.g., it is not always relieved by nitroglycerin, not always brought on by exertion, or relieved after 15 to 20 minutes of rest), and **nonanginal chest pain** lacks all features of typical angina (i.e., it is unrelated to activity, unrelieved by nitroglycerin, or otherwise not suggestive of angina).

C. HAND GESTURES DURING DESCRIPTION OF CHEST PAIN

According to traditional teachings, patients provide diagnostic clues to the physician by the hand gestures they spontaneously make when describing their chest pain. Four of these gestures are: (1) **Levine sign**—placing clenched fist against the sternum, (2) **palm sign**—placing the extended palm against the sternum, (3) **arm sign**—gripping the left arm, and (4) **pointing sign**—pointing to a single point on the chest with one or two fingers.[18] According to traditional teachings, gestures suggesting deep, poorly localized visceral pain (Levine and palm signs) or pain radiating to the left arm (arm sign) increase the probability of coronary disease, whereas gestures indicating well-localized somatic pain (pointing sign) decrease the probability of disease.

*Heberden based the term *angina* on the Greek *agkhone*, which means "strangling." This Greek root also forms the basis for the English words *anxiety* and *anguish*. Heberden's selection of *angina* was unfortunate because the term had already been applied to other conditions of the throat, such as Vincent *angina* and Ludwig *angina*.

D. PHYSICAL FINDINGS

Some of the findings that appear in EBM Boxes 49.1 and 49.2 are discussed in other chapters: crackles (Chapter 30), displaced precordial pulsation (Chapter 38), and the third heart sound (Chapter 41).

1. EARLOBE CREASE

The earlobe crease is a diagonal crease across the earlobe, connecting the lowest point on the tragus to the outside of the earlobe (Fig. 49.1). Some investigators define the finding as a crease traversing at least one-third the distance from tragus to posterior pinna,[37,38] whereas others require the crease to extend the total distance.[29,32,39] In a letter to the editor written in 1973[72] Frank first presented the "positive earlobe sign" as a sign tightly associated with other cardiovascular risk factors. Although its association with coronary disease remains controversial and its pathogenesis a mystery, many investigators have shown that the earlobe crease is a modest risk factor for coronary artery disease, independent of other traditional risk factors, such as hypertension, age, diabetes mellitus, family history, hyperlipidemia, obesity, and cigarette smoking.[32,37,39,73,74]

2. ARCUS SENILIS

Arcus senilis is a white or grayish opaque ring about the circumference of the cornea. Since the 1830s this sign has been associated with both older age (hence "senilis") and vascular disease (Virchow considered it a definite sign of heart disease).[75] Modern investigators[76,77] continue to suggest arcus senilis is linked to coronary disease, independent of its association with hyperlipidemia, although others challenge this view.[75]

3. ANKLE-TO-ARM PRESSURE INDEX

After positioning the patient supine, the clinician uses a handheld Doppler stethoscope to measure the highest systolic blood pressure in the posterior tibial or dorsalis pedis artery (i.e., the "ankle" pressure). The **ankle-to-arm pressure index** represents this ankle pressure divided by the systolic pressure in the brachial artery (see Chapter 54).

E. GI COCKTAIL

For many years, clinicians working in emergency departments have mixed liquid antacids with other substances (most commonly viscous lidocaine, a topical anesthetic, and an elixir with the trade name of Donnatol, an antispasmotic) to create **GI cocktails**, which are administered orally to patients presenting with chest or upper abdominal discomfort. Because GI cocktail should act topically only on GI mucosa, prompt relief of a patient's discomfort is said to support a GI cause of pain (and, by inference, argue against a cardiac cause of the pain). Although antacid, lidocaine, and Donnatol are the standard ingredients of GI cocktail, some investigators have shown that antacid alone (without lidocaine or Donnatol) may relieve pain just as well.[78]

III. CLINICAL SIGNIFICANCE

A. DIAGNOSING CORONARY ARTERY DISEASE

EBM Box 49.1 summarizes the accuracy of bedside findings in diagnosing coronary artery disease (based on study of more than 10,000 patients).[79] Almost all of the patients in these studies presented to outpatient clinics with intermittent chest pain, and the diagnosis of coronary artery disease was based on subsequent cardiac

EBM BOX 49.1
*Coronary Artery Disease**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Patient Interview				
Description of Chest Pain				
Classification of chest pain[19-26]				
Typical angina	50-91	78-94	**5.8**	—
Atypical angina	8-44	—	1.2	—
Nonanginal chest pain	4-22	14-50	**0.1**	—
Pain duration >30 min[27]	1	86	**0.1**	NS
Associated dysphagia[27]	5	80	**0.2**	NS
Other				
Male sex[24,25,28-33]	72-86	36-58	1.7	**0.3**
Age[25,28-30,33,34]				
<30 years	0-1	97-98	NS	—
30-49 year	16-38	—	0.6	—
50-70 years	62-73	—	1.3	—
>70 years	2-52	67-99	2.6	
Prior myocardial infarction[24,26,30,31,33,35,36]	42-69	66-99	**3.8**	0.6
Physical Examination				
Earlobe crease[29,32,37-41]	26-80	33-96	2.3	0.5
Arcus senilis[42]	40	86	**3.0**	0.7
Chest wall tenderness[27,43-45]	1-69	16-97	0.8	NS
Ankle-to-arm pressure index <0.9[46,47]	20-26	93-95	**4.0**	0.8
Laterally displaced apical impulse[48]	5	100	NS	NS
Electrocardiogram				
Normal[26,48,49]	15-33	50-69	NS	NS
ST/T wave abnormalities[19,26,36]	14-44	73-93	NS	NS

*Diagnostic standard: for *coronary artery disease*, coronary angiography reveals greater than 50%,[20,22-24,26,28,29,32,34,35,37-40,42,44,46,47,49] >60%,[48] or >70% to 75%[19,21,25,27,30,31,33,36,41] stenosis of any epicardial vessel or positive myocardial perfusion scan.[45]
†Definition of findings: for classification of chest pain, earlobe crease, and arcus senilis, see the text.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
NS, Not significant.
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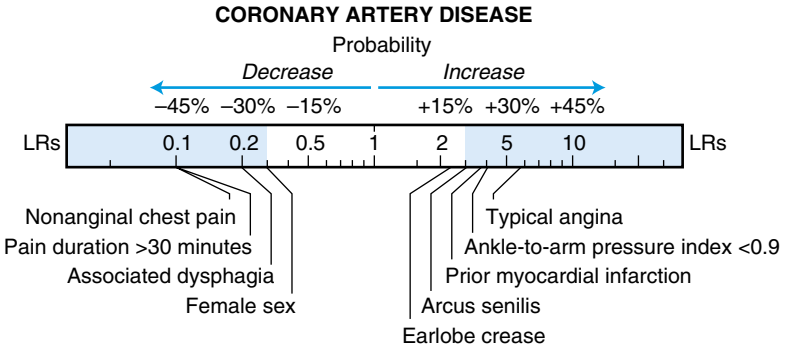

catheterization revealing a significant stenosis (>50% to 70% luminal narrowing) in any major epicardial vessel (i.e., single-vessel disease or worse).

According to the likelihood ratios (LRs) in EBM Box 49.1 the findings *increasing* the probability of coronary disease the most in patients with intermittent chest pain are typical angina (LR = 5.8), ankle-to-arm pressure index of less than 0.9 (LR = 4), previous myocardial infarction (LR = 3.8), arcus senilis (LR = 3), age older than 70 years (LR = 2.6), and a positive earlobe crease (LR = 2.3).

These studies confirm Heberden's original impression that the key diagnostic finding in patients with chest pain is the patient's actual description of pain. Many investigators have attempted to improve on Heberden's definition of typical angina by dissecting apart the individual components of the patient's description (e.g., response to nitroglycerin or the pain's quality) or by creating complicated angina scoring schemes, but each of these attempts to improve diagnosis is less accurate than the clinician's global perception of whether the patient's pain is typical angina or not.[79]

The findings that *decrease* the probability of coronary artery disease in these studies are chest pain that is nonanginal (i.e., pain unrelated to activity, unrelieved by nitroglycerin, or otherwise not suggestive of angina, LR = 0.1), pain duration longer than 30 minutes (LR = 0.1), and associated dysphagia (LR = 0.2).

Unhelpful findings include atypical angina, chest wall tenderness, and a displaced apical impulse. Additional descriptors of the pain, such as burning pain, pain made worse by food or emotion, and radiation of the pain to the arms, are also unhelpful (i.e., they appear just as often in patients with coronary disease as in patients with noncardiac chest pain, and the LRs are not different from the value of 1).[79] Neither the Levine sign nor the palm sign affects the probability of coronary disease.[80] Interestingly, electrocardiographic findings (i.e., normal vs. abnormal, presence or absence of nonspecific ST changes) also are diagnostically unhelpful in these studies (LR not significant; see EBM Box 49.1).

Assessment of the patient's traditional risk factors—hypertension, diabetes mellitus, cigarette smoking, family history, or combinations of these—carry much less diagnostic weight than the patient's description of pain. Each of these risk factors—except for cholesterol level higher than 300 mg/dL (LR = 4) and cholesterol level lower than 200 mg/dL (LR = 0.3)—has an LR between the values of 1.2 and 2.3, thus changing probability of disease little if at all.[79,81,82] Even combinations of three or more risk factors change probability of coronary disease relatively little (LR = 2.2, a value similar to the LR for the earlobe crease).[79]

EBM BOX 49.2
*Myocardial Infarction**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Patient Interview				
Male sex[50-59]	59-72	24-61	1.3	0.7
Age[50,55,56]				
<40 years	4	81	**0.2**	—
40-59 years	34	—	NS	—
≥60 years	47-74	54-68	1.5	—
Sharp pain[55,60,61]	8-19	59-72	0.4	1.3
Pleuritic pain[55,56,60,61]	3-19	69-82	**0.3**	1.2
Positional pain[55,56,61]	3-14	75-87	0.4	1.1
Relief of pain with nitroglycerin[62-65]	35-92	12-59	NS	NS
Physical Examination				
Hand gestures[18]				
Levine sign	7	87	NS	NS
Palm sign	32	63	NS	NS
Arm sign	18	83	NS	NS
Pointing sign	2	95	NS	NS
Chest wall tenderness[55,56,60,61]	3-15	64-83	**0.3**	1.2
Diaphoretic appearance[56,59,60]	28-56	71-94	2.2	0.7
Pallor[59]	70	49	1.4	0.6
Systolic blood pressure <100 mm Hg[52]	6	98	**3.6**	NS
Jugular venous distention[51]	10	96	2.4	NS
Pulmonary crackles[51,60]	20-38	82-91	2.1	NS
Third heart sound[60]	16	95	**3.2**	NS
Electrocardiogram				
Normal[50,52,55,59,66-69]	1-13	48-77	**0.2**	1.5
Nonspecific ST changes[55,59,68]	5-8	47-78	**0.2**	1.4
ST elevation[52,59,60,67,68,70,71]	31-56	97-100	**22.3**	0.6
ST depression[52,59,60,67,68]	20-62	79-96	**3.9**	0.8
T wave inversion[52,59,60,67]	9-39	84-94	2.0	NS

*Diagnostic standard: for *myocardial infarction,* development of new electrocardiographic Q waves, elevations of cardiac biomarkers (CK-MB or troponin), or both; except for the studies of nitroglycerin effect, which used a broader definition of "active coronary disease" that combined myocardial infarction, positive stress test, or abnormal coronary arteriogram.[62-64]

†Definition of findings: for *relief of pain with nitroglycerin*, nitroglycerin provided moderate or complete relief within. All electrocardiographic abnormalities refer to findings that are new or of unknown duration.

‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR

NS, Not significant.

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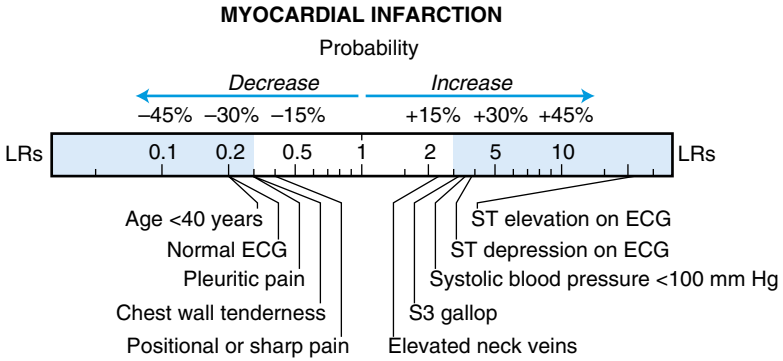

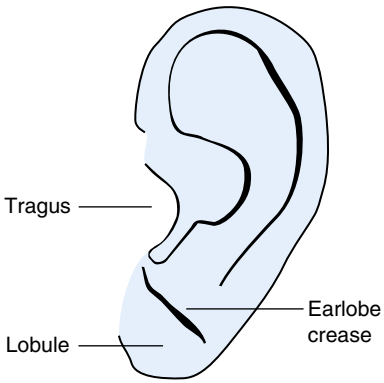

FIG. 49.1 EARLOBE CREASE. The earlobe crease is a diagonal crease extending from the lowest point on the tragus to the outside of the earlobe. See the text.

B. DIAGNOSING MYOCARDIAL INFARCTION

EBM Box 49.2 summarizes the findings in thousands of patients presenting to emergency departments with sustained acute chest pain unrelated to trauma and unexplained by the chest radiograph. The diagnosis of myocardial infarction was confirmed by the development of new Q waves on the electrocardiogram, elevations of cardiac biomarkers (CK-MB or troponin), or both.

According to the LRs in Table 45.2, the finding *increasing* the probability of myocardial infarction the most is new electrocardiographic ST elevation (LR = 22.3) or ST depression (LR = 3.9). Several additional physical findings have modest value in diagnosing myocardial infarction: systolic blood pressure lower than 100 mm Hg (LR = 3.6), a third heart sound (LR = 3.2), jugular venous distention (LR = 2.4), diaphoretic appearance (LR = 2.2), and pulmonary crackles (LR = 2.1). Radiation of pain to the right arm (LR = 2.7) increases probability of myocardial infarction more than radiation to the left arm (LR = 1.5).[50,51,60,61,79,83,84] The only findings *decreasing* the probability of myocardial infarction in these studies are pain that is pleuritic (LR = 0.3), positional (LR = 0.4), or sharp (LR = 0.4); a normal electrocardiogram (LR =

0.2); chest wall tenderness (LR = 0.3); and age younger than 40 years (LR = 0.2). In another study of 1635 patients presenting with chest pain to emergency departments, the finding of chest wall tenderness (reproducing the patient's pain) greatly decreased the probability of acute coronary syndrome (i.e., myocardial infarction or unstable angina) during the next 30 days (LR = 0.1).[85]

The response to nitroglycerin fails to discriminate between cardiac and noncardiac causes of chest pain (LR not significant; see EBM Box 49.2). This may reflect the temporary nature of most chest pain or perhaps the noncardiac effects of nitroglycerin. Nonetheless, even though the response to nitroglycerin lacks diagnostic value in patients with sustained chest pain, it remains a key element in the definition of typical angina. (See the previous discussion in the section on Description of Chest Pain.)

The different hand signs also lack diagnostic value in studies of patients admitted with chest discomfort (see EBM Box 49.2).

One interesting contrast between the diagnosis of coronary disease (see EBM Box 49.1) and myocardial infarction (see EBM Box 49.2) is that chest wall tenderness decreases the probability of myocardial infarction (LR = 0.3; see EBM Box 49.2) but lacks diagnostic value when considering coronary artery disease (LR = 0.8; see EBM Box 49.1). This difference may reflect a higher prevalence of chest wall disorders in patients without disease in the acute chest pain studies.

C. RISK FACTORS AND CORONARY DISEASE

In patients with sustained chest pain, the presence or absence of traditional cardiovascular risk factors again carries little or no diagnostic weight (positive LRs = 1.2 to 1.7).[79] There are two important reasons why risk factors fail to discriminate well in diagnostic studies. First, traditional cardiovascular risk factors are mostly derived from study of middle-aged white residents of Framingham, Massachusetts.[86] They may thus overestimate the risk in other populations, something that has been demonstrated in British men,[87] elderly Americans,[88] and Japanese-American, Native American, and Hispanic populations.[89] A second reason is the fundamental difference between risk factors and diagnostic signs. Risk factors precede disease, presumably play a role in causing the disease, and become apparent only after study of large groups of *asymptomatic* individuals for long periods of time. In contrast, diagnostic signs first appear after the onset of disease, are *caused by* the disease, and become evident after study of a relatively smaller group of *symptomatic* individuals. For example, it is possible that certain risk factors associated with coronary disease are also associated with noncardiac causes of pain, which would neutralize any diagnostic value (e.g., cigarette smoking may also increase the risk of chest wall pain, making it appear just as often in patients with noncardiac pain as those with cardiac pain. The resulting LR would therefore have a value near 1.).

D. GI COCKTAIL

The existing literature suggests that the GI cocktail has questionable diagnostic value. One problem is that clinicians usually administer the GI cocktail just minutes away from other active medications, such as narcotics, nitroglycerin, antiemetics, histamine blockers, or ketorolac, thus clouding interpretation of the test's results.[90] Another problem is that the viscous lidocaine is absorbed, and even though most patients have levels below 1 μg/mL (usual therapeutic levels are 2 to 5 μg/mL), instances of toxicity and seizures have occurred.[90-92] A final and most troubling problem is the many documented examples of GI cocktail relieving the discomfort of disorders distant from the gastroesophageal mucosa, such as myocardial infarction,[91,93] hepatitis, pancreatitis, or cholecystitis.[94]

E. PROGNOSIS AND ACUTE CHEST PAIN

In patients with acute chest pain, clinicians are interested in diagnosing more than just myocardial infarction because many acute coronary syndromes *without* infarction are also associated with life-threatening complications that require intensive monitoring and treatment. To identify all patients at risk for such complications, Goldman has developed a rule that assesses the patient's electrocardiogram and the presence or absence of three additional bedside findings: (1) systolic blood pressure of less than 110 mm Hg, (2) crackles heard above the bases bilaterally, and (3) chest pain that is either worse than prior angina, the same as prior myocardial infarction, or occurs in the post-infarction or post-revascularization setting.[95] According to this rule, patients have a "high risk" of life-threatening complications in the first 24 hours of hospitalization if there is either (1) electrocardiograph ST elevation or Q waves (not known to be old) *or* (2) electrocardiographic ST depression or T wave inversion (not known to be old) *and* two or more of the three bedside findings. Patients are classified as "very low risk" if their electrocardiogram reveals no ST/T wave changes or Q waves and they lack all three bedside findings.

EBM Box 49.3 indicates that in patients with acute chest pain a "high risk" classification increases the likelihood of life-threatening complications in the subsequent 24 hours (LR = 8.7; see EBM Box 49.3), whereas a "very low risk" classification

EBM BOX 49.3
*Predicting Life-Threatening Complications in Patients With Acute Chest Pain**

Finding (Reference)†	*Sensitivity (%)*	*Specificity (%)*	Likelihood Ratio‡ if Finding Is	
			Present	*Absent*
Goldman Classification				
"High" risk[95,96]	51-88	92-93	**8.7**	—
"Very low" risk[95-97]	7-13	42-53	**0.1**	—

*Diagnostic standard: for *life-threatening complications,* any of the following during the first 24 hours of hospitalization: arrhythmias (ventricular fibrillation, cardiac arrest, new complete heart block, insertion of temporary pacemaker, emergency cardioversion), pump failure (cardiogenic shock, use of intra-aortic balloon pump, intubation), or ischemia (recurrent ischemic chest pain requiring bypass surgery or percutaneous intervention).[95]
†Definition of findings: for *high risk* and *very low risk*, see the text.
‡Likelihood ratio (LR) if finding present = positive LR; LR if finding absent = negative LR.
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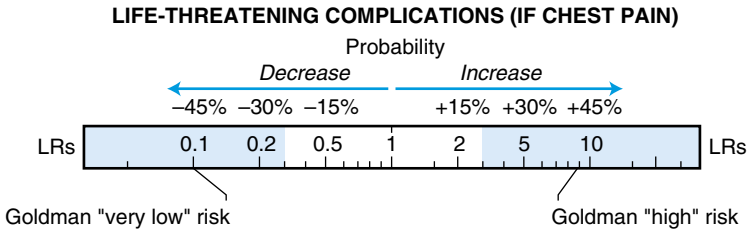

indicates a favorable prognosis (LR = 0.1; see EBM Box 49.3). This rule compares favorably with the diagnostic accuracy of elevated troponin T levels, drawn at least 6 hours after the onset of chest pain in patients without ST elevation, in predicting cardiac events in the subsequent 30 days (positive LR = 6.1, negative LR = 0.2).[98]

The references for this chapter can be found on www.expertconsult.com.

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